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10/505,213	11/22/2004	Suzanne Margaret Price	114.1007	5907

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EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,213	PRICE, SUZANNE MARGARET	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-64* is/are pending in the application.

4a) Of the above claim(s) *43-58 and 61-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on July 1, 2010 has been entered.

2. Applicant's arguments and amendments to the claims have been fully considered but are not persuasive to place all claims in condition for allowance. All rejections not reiterated herein are hereby withdrawn. In particular, the previous rejection of claims 12, 13 and 15-19 under 35 U.S.C. 112, second paragraph has been obviated by the cancellation of these claims.

This action contains new grounds of rejection and is made non-final.

Election/Restrictions

3. Claims 43-58 and 61-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 12, 2007.

It is noted that the claims filed on August 19, 2004 were subject to a restriction requirement and a requirement to elect a particular species, as set forth in the Office

action of February 9, 2007. The claims included generic claim 1 directed to a method of analyzing a nucleic acid sample obtained from a site comprising the step of pretreating the sample to remove or inactivate contaminating nucleic acids originating from the site. The claims also included, e.g., claim 8 directed to a method which recited species and particularly recited that the pre-treatment is one or more treatments selected from enzymic treatments, physical treatments and chemical treatments. In response to the requirement to elect a particular species, Applicant elect the single species of enzymic treatments in the response of March 12, 2007. Note that Applicants did not elect chemical or physical treatments, or the combination of chemical and enzymic and/or physical treatments. Only present claims 59 and 60 read on the elected invention of a method of analyzing a nucleic acid which method requires pretreatment of a sample with an enzyme. Claims 43-58 and 61-63 are directed to the non-elected species of methods that require chemical and physical treatments to inactivate and remove contaminating nucleic acids. These claims are withdrawn from consideration since there are not currently any allowable linking or generic claims.

Regarding newly added claim 64, this claim is directed to a database comprising results generated by the method of claim 43. This invention does not share a special technical feature with the elected invention of methods of analyzing a nucleic acid by treating a sample to remove contaminating nucleic acids and then analyzing the sample. The technical feature of methods of analyzing a nucleic acid by treating a sample to remove contaminating nucleic acids and then analyzing the sample was known in the art at the time the invention was made and was specifically taught by

Walker, Satishchandran and Miwa as set forth in paragraphs 6-8 below. Accordingly, there is no special technical feature linking the claimed inventions as would be necessary to fulfill the requirement for unity of invention.

Claim Rejections - 35 USC § 112 second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 59 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 59 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps is the steps of removing contaminating nucleic acid and analyzing the sample. That is, the claims are drawn to method for removing contaminating nucleic acids from a sample and then analyzing the sample. However, the claims recite only a step of treating the sample to inactivate contaminating nucleic acids. The claims do not recite any steps of analyzing the sample. Moreover, the claims do not recite a clear step of removing contaminating nucleic acids. The claims recite only a step of inactivating a nucleic acid. The inactivation of a nucleic acid is not equivalent to the removal of a nucleic acid. The claims do not set forth a relationship between the inactivation of the contaminating nucleic acid and the removal of the contaminating nucleic acid. In the absence of clear nexus between the inactivation and

removal of contaminating nucleic acids, the claims appear to also omit the essential process step of removing contaminating nucleic acids.

Claim 60 is indefinite over the recitation of "enzymatic treatment requires the use of." This language is vague and renders the claim indefinite because it is unclear as to whether the treatment includes performing an active process step using a methylation specific enzyme or if it is only a property of the enzymatic treatment that it does, under some unstated conditions, involve or otherwise utilizes methylation specific restriction enzyme. In the latter case, the claims do not recite the criteria or conditions for how the methylation specific restriction enzyme is used for treatment. Therefore, one cannot determine the meets and bounds of the claimed subject matter. Note that MPEP 2773.02 states that if the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 USC 112, second paragraph, is appropriate.

Claim Rejections - 35 USC § 112, first paragraph – New Matter

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 60 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the recitation in newly added claim 60 that the enzymatic treatment requires the use of methylation specific restriction enzymes.

In the response of July 1, 2010, Applicants point to page 6, line 5 to page 7, line 22 as providing support for claim 60. However, the cited teachings in the specification provide support only for the concept of treating the sample with enzymes that preferentially breakdown nucleic acids, such as DNases, RNAses, exonucleases and endonucleases. The specification does not teach using the particular endonuclease of a methylation specific restriction enzyme.

As set forth in MPEP 2163.05, the written description requirement prevents an applicant from claiming subject matter that was not adequately described in the specification as filed. New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. Further, MPEP 21603.05 states that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) . In the present situation, the disclosure of the genus of treatment with endonucleases does not provide support for the particular species of treatment with methylation specific restriction enzymes.

Maintained Rejections

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 59 is rejected under 35 U.S.C. 102(b) as being anticipated by Walker (EP 0585660; cited in the IDS).

The following grounds of rejection was previously presented in the Office action of June 1, 2009 and has been modified herein to address the amendments to the claims.

Walker teaches a method for removing contaminating nucleic acids from a sample and then analyzing the sample wherein the method comprises: i) treating a nucleic acid sample with a single-strand specific exonuclease to remove or inactivate contaminating nucleic acids; ii) contacting the sample with a primer; and iii) amplifying the treated sample to thereby analyze the nucleic acid sample (see, e.g., page 2, lines 24-57 and page 4, lines 43-46). In the method of Walker, the step of treating the nucleic acid sample with a single-strand specific exonuclease constitutes a step of enzymatic treatment to inactivate contaminating nucleic acids because treatment with single-strand specific exonuclease removes or inactivates nucleic acids produced by other amplification processes and thereby removes or inactivates nucleic acids that are free or substantially free of other cell components. It is noted that in the method of Walker,

the sample is contaminated with laboratory derived nucleic acids and digestion with the single-strand specific exonuclease removes contaminating single-stranded nucleic acids from the sample prior to analysis.

Response to Remarks:

In the response of July 1, 2010, Applicant's traversed this rejection by stating that:

> The Walker patent teaches an amplicon decontamination method comprising combining a nucleic acid preparation containing target nucleic acid (which may be contaminated with amplicons [contaminating nucleic acids]) with a single strand specific exonuclease. The mixture is then incubated for a sufficient time to degrade the amplicons. This is clearly set out on page 2, lines 24- 30 of the document, under "Summary of the Invention". The Walker Patent neither teaches nor suggests that the treatment step is a chemical modification of the contaminating nucleic acids, which renders them removable from the sample, in contrast to the independent claims of the present application set forth above.

This argument has been fully considered but is not persuasive because it is directed to limitations that are not recited in claim 59. Specifically, claim 59 does not require chemical modification of a nucleic acid which renders the nucleic acid removable from the sample.

The response further states that "the aim of the method of the present invention is to completely degrade the amplicons, not render them removable from the sample using a primer or probe." This argument has also been fully considered but is not persuasive because the present claims do not require complete degradation of a nucleic acid and particularly of an amplicon. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The response goes on to discuss examples 2-6 of the specification and characterizes the examples as illustrating methods of treating a sample with an exonuclease for a determined period of time, including incubation for 22 minutes with an exonuclease. It is stated that the method further shows the use of primers of SEQ ID NO: 1-4 to amplify target DNA and that the primers were not associated with the amplicons.

These arguments have been fully considered but it is unclear as to how these arguments pertain to present claim 59. Claim 59 does not require treatment with an exonuclease for a particular period of time, such as 22 minutes. Nor does claim 59 require amplification with a primer. The method of claim 59 requires only a step of enzymatically treating the sample. This method is disclosed by Walker since Walker teaches treatment of the sample with a single-strand specific exonuclease enzyme to digest and thereby remove contaminating nucleic acids prior to analysis of the sample.
7. Claims 59 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Satishchandran et al (U.S. Patent No. 6,168,918).

The following rejection was previously presented in the Office action of June 1, 2009 and has been modified herein to address the amendments to the claims.

Satishchandran teaches a method comprising: i) treating a nucleic acid sample with DpnI restriction endonuclease to remove or inactivate contaminating plasmid nucleic acids present in the sample; and ii) analyzing the treated sample (see, e.g., col. 5, lines 29-67; col. 7, lines 28-67). Satishchandran teaches that DpnI cleaves GATC sequences if the adenine is methylated and the adenine nucleotide will be methylated if

plasmid DNA is synthesized in Dam+ cells (col. 4, line 58 to col. 5, line 28). Thus, in the method of Satishchandran, treatment of the sample with DpnI results in the digestion (inactivation and removal) of contaminating plasmid DNA because the plasmid DNA is methylated. Accordingly, Satishchandran anticipates the claimed method since Satishchandran teaches a method comprising the step of enzymatically treating the sample, wherein the enzymatic treatment results in the inactivation of the contaminating nucleic acid.

Regarding claim 60, the treatment step of Satishchandran comprises treating the nucleic acid sample using the enzyme DpnI which is a methylation specific (sensitive) restriction endonuclease (e.g., col. 1, lines 43-56; col. 4, lines 58-65).

Response to Remarks:

In the response of July 1, 2010, Applicants state that the "Satishchandran patent is directed towards a method that tests whether or not foreign DNA is integrated into the chromosomal DNA of a eukaryote cell. It is not directed towards a method of chemically treating a sample to preferentially chemically modify the contaminating nucleic acids."

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., chemically treating a sample to preferentially chemically modify the contaminating nucleic acids) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The response further states that Satishchandran describes "the use of DpnI to selectively cleave free plasmid DNA molecules in the presence of genomic DNA which might contain integrated plasmid sequences. This step is specifically designed to remove non-integrated DNA molecules by enzyme digestion. These DNA molecules (which might be considered by the Examiner to be 'contaminating' nucleic acids), are not the subject of chemical treatment."

This argument has also been fully considered but is not persuasive because the present claims do not require a chemical treatment. Rather, the claims require treatment with an enzyme and particularly a methylation specific restriction enzyme. As set forth above, Satishchandran teaches the steps required by the present claims since Satishchandran teaches a method comprising treating a sample with the methylation specific restriction enzyme DpnI to digest and thereby remove contaminating nucleic acids, and then analyzing the nucleic acids that remain in the sample.

8. Claim 59 is rejected under 35 U.S.C. 102(b) as being anticipated by Miwa (U.S. Patent No. 4,514,502; cited in the Office action of 6/11/07).

The following rejection was previously presented in the Office actions of 6/11/07, 1/4/08 and 9/19/08 and now applies herein to newly added claim 59.

Miwa teaches a method for removing contaminating nucleic acids from a sample and then analyzing the sample wherein the method comprises: i) treating a nucleic acid sample with the enzyme RNase to remove or inactivate contaminating RNA (i.e., nucleic acids) from the sample; and ii) analyzing the treated sample (see, e.g., col. 6, lines 56-68 through col. 7, lines 1-6 and 48-51). In the method of Miwa, the step of treating the

sample with RNase constitutes a step of enzymatically treating the sample to remove or inactivate contaminating RNA because treatment with RNase digests RNA present in the sample.

New Grounds of Rejection:

9. Claim 59 is rejected under 35 U.S.C. 102(b) as being anticipated by Longo et al. Gene. 1990. 93: 125-128).

Longo teaches a method comprising: i) treating a nucleic acid sample with the enzyme uracil DNA glycosylase (UDG) to inactivate contaminating nucleic acids (i.e., amplicons from prior amplification reactions which contain uracil); and ii) analyzing the treated sample (see, abstract, Figures 1 and 2; page 126 to page 127, col. 1). In the method of Longo, the step of treating the sample with uracil DNA glycosylase constitutes a step of enzymatically treating the sample to inactivate contaminating nucleic acid because treatment with uracil DNA glycosylase removes uracil from the phosphodiester backbone of uracil-containing DNA. Longo teaches that the resulting apyrimidinic sites block replication by DNA polymerase and are very labile to acid/base hydrolysis (see abstract and page 126). Thereby, nucleic acids that contain uracil, such as PCR products from prior reactions in which uracil was incorporated into the amplicons, will have their uracils removed by UDG, blocking their re-amplification while leaving nature DNA containing thymine bases unaffected (page 126).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/

Primary Examiner, Art Unit 1634